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Attorney's Do. No. 4430-18

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Andrew D. Barofsky &amp; Kenton W. Gregory

Serial No. 08/797,770 Group Art Unit: 3738

Filing Date: February 7, 1997 Examiner: Paul Prebilic

For: METHOD FOR USING TROPOELASTIN AND FOR PRODUCING  
TROPOELASTIN BIOMATERIALSAssistant Commissioner for Patents  
Washington, D.C. 20231DECLARATION OF PRIOR INVENTION IN THE UNITED STATES  
TO OVERCOME A CITED PUBLICATION (37 C.F.R. 1.131)

1. This declaration is to establish completion of the invention in this application in the United States, at a date prior to May 23, 1996, that is the effective date ("Effective Date") of the prior art publication WO 96/14807 to Gregory, et al ("Reference"), that was cited by the Examiner.
2. The persons making this declaration are the inventors.
3. To establish the date of conception of the invention of this application, the following attached document is as evidence:

Exhibit A Relevant descriptions of the invention of Mr. Barofsky and Dr. Gregory which were included in a confidential Research Proposal submitted prior to the Effective Date.

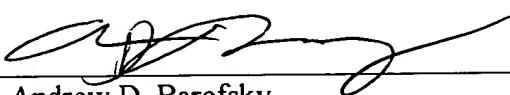
4. This document evidences that the invention in this application was conceived at least by a date earlier than the Effective Date of the Reference.
5. Work on tropoelastin was conducted continuously from a date prior to the Effective Date until the date of filing of the above referenced patent application, and thereafter.
6. This declaration is submitted with the first response after final rejection, and is for the purpose of overcoming a new ground of rejection or requirement made in the final rejection.

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We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Inventor's signature



Dated:

6/23/99

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### Tropoelastin Biopolymers

Vascular grafts utilizing the human elastin precursor, tropoelastin, that is polymerized and molded into dimensions exactly as specified, having drugs incorporated where needed, may be the optimal biomaterial for vascular replacement and repair. Presently, substantial technical obstacles must be overcome if this material can be produced in any reasonable quantity. Considering the interval between initiation of basic studies and routine deployment in patients being at least 5-10 years, we propose to initiate basic developmental work identifying processes for obtaining tropoelastin in the first year of this proposal.

Currently, the most common method of obtaining tropoelastin is by extracting the protein from elastin rich tissues of lathyritic or copper deficient animals [34,35]. In both cases the diet induced inhibition of lysyl oxidase leads to the accumulation of tropoelastin in quantities sufficient for effective extraction. Alternatively, a few groups have reported the successful production of recombinant human tropoelastin in bacterial (E. Coli) expression systems. Unfortunately, yields of tropoelastin from both tissue extraction and bacterial expression systems still remain too low for production of bioartificial tissue.

This project requires large scale production of biologically active tropoelastin.



Tropo-elastin sheets and conduits will be evaluated for suitability for vascular implants. Strength, elasticity, tear strength, thermal stability, durability of various formulations will be evaluated.